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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/750,972	12/28/2000	Pramod K. Srivastava	8449-134	7769

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EXAMINER
YAEN, CHRISTOPHER H

ART UNIT	PAPER NUMBER
1642	19

DATE MAILED: 12/04/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/750,972	SRIVASTAVA, PRAMOD K.	
	Examiner	Art Unit	
	Christopher H Yaen	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 September 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *75,97,99-101,104-112,121,122 and 129-132* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *75,97,99-101,104-112,121,122 and 129-132* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *18* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. The amendment filed 9/5/02 (paper no. 17) is acknowledged and entered into the record. Accordingly, claims 98, 102-103, 113-120, and 123-128 are canceled without prejudice, claims 75, 97, 99-101, 104, 105, 107, 108, 110, 111, 121, and 122 are amended, and claims 129-132 are newly added. Therefore, claims 75, 97, 99-101, 104-112, 121-122, and 129-132 are pending and examined on the merits.

Information Disclosure Statement

2. The Information Disclosure Statement filed 9/5/02 (paper no. 18) is acknowledged and considered. A signed copy of the IDS is attached hereto.

Petition to Correct Inventorship

3. In view of the papers filed 8/13/02, it has been found that this nonprovisional application, as filed, through error and without deceptive intent, improperly set forth the inventorship, and accordingly, this application has been corrected in compliance with 37 CFR 1.48(a). The inventorship of this application has been changed by adding Robert J. Binder.

The application will be forwarded to the Office of Initial Patent Examination (OIPE) for issuance of a corrected filing receipt, and correction of the file jacket and PTO PALM data to reflect the inventorship as corrected.

Claim Rejections Withdrawn – 35 USC § 112, 1st paragraph

4. The rejection of claims 75, and 97-128 under 35 USC 112, 1st paragraph as lacking enablement for all purified compounds is withdrawn in view of the arguments and amendments to the claims set forth by the applicant.

5. The rejection of claims 97,98,102,115,117, and 126 under 35 USC 112, 1st paragraph as lacking enablement for all HSP is withdrawn in view of the arguments and amendments to the claims set forth by the applicant.

Claim Rejections Withdrawn-35 USC§ 102

6. The rejection of claims 75, 97, 104-105, 107-108, 110-111, 113, 122, and 123 under 35 USC 102 (b) as being anticipated by Pizzo (WO 94/14976) is withdrawn in view of the amendments and arguments set forth by the applicant.

Claim Rejections Withdrawn-35 USC§ 103

7. The rejection of claims 75, 97, 103-114, 116, 122-123, and 127 under 35 USC 103 (a) as being obvious over by Pizzo (WO 94/14976) in view of Isaacs *et al* (j. Biol Chem 1988 May;263(14):6709-6714) is withdrawn in view of the amendments and arguments set forth by the applicant.

Claim Rejection Maintained- 35 USC§ 112, 1st paragraph

8. The rejection of claim 121 under 35 USC 112, 1st paragraph as lacking proper written description is maintained for the reasons of record. Applicant argues that the amendment of the claims to recite that an antiCD91 antibody is an agonist will render the rejection moot was carefully considered but is not found persuasive for the following reason. The specification only specifically teaches an antibody that is capable of inhibiting and not enhancing the activity of a receptor. Any one of skill in the art would know that agonists enhance activity of a receptor. As such there is not disclosure that one of skill in the art would find in the specification to lead them to believe that at the

time of filling, applicant was in possession of an antibody that was capable of enhancing the activity of CD91/alpha 2 macroglobulin receptor.

New Claim Rejections 35 USC§ 112, 2nd paragraph

9. Claims 75, 97, 99-101, 104-112, 121-122, and 129-132 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

10. Regarding claim 75, 104-105, 107, 110, and dependent claims thereof, in the recitation of "preventing" or "prevent", it is unclear as to how such a method is capable accomplishing the desired task.

11. Regarding claims 75, 105, and dependent claims thereof, in the recitation of the phrase "amount effective", it is unclear as to the amount referred. As such the metes and bounds of the term cannot be determined because any amount can be considered effective.

12. Regarding claims 97, 105, 108, 111, and dependent claims thereof in the recitation of the term "modulate", it is unclear as to whether this term represents an inhibition or an enhancement of activity.

13. Regarding claim 105, 108, 111, and dependent claims thereof in the recitation of the term "ligand", it is unclear as to which ligand is being referred. As such the metes and bounds of the term cannot be determined, because there are a multitude of possible ligands that can interact with CD91.

14. Regarding claims 97, 99, 100, 101 in the recitation of the terms "heat shock proteins", it is unclear as to what type of Hsp is being referred, the metes and bounds of

the term cannot be determined because there are numerous Hsps; in the recitation of the terms "gp96", "Hsp70", and "Hsp90", it is unclear as to whether these are derived from humans or from bacteria.

New Claim Rejections 35 USC§ 112, 1st paragraph

15. Claims 75, 97, 99-101, 104-112, 121-122, and 129-132 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The first paragraph of 35 U.S.C. 112 states, "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same...". The courts have interpreted this to mean that the specification must enable one skilled in the art to make and use the invention without undue experimentation. The courts have further interpreted undue experimentation as requiring "ingenuity beyond that to be expected of one of ordinary skill in the art" (Fields v. Conover, 170 USPQ 276 (CCPA 1971)) or requiring an extended period of experimentation in the absence of sufficient direction or guidance (In re Colianni, 195 USPQ 150 (CCPA 1977)). Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Colianni, 195 USPQ 150, 153 (CCPA 1977) and have been clarified by the Board of Patent Appeals and Interferences in Ex parte Forman, 230 USPQ 546 (BPAI 1986). Among

the factors are the nature of the invention, the state of the prior art, the predictability or lack thereof in the art, the amount of direction or guidance present, the presence or absence of working examples, the breadth of the claims, and the quantity of experimentation needed.

The nature of the invention: The claims of the instant invention are drawn to a method of treating or preventing an autoimmune disorder, prolifertive disorder, or infectious disease comprising the administration of an anti-CD91 antibody.

The state of the prior art and the predictability or lack thereof in the art: The art teaches that CD91 or alpha 2 macroglobulin receptor is the receptor for HSP 70, HSP 90, gp96, and calreticulin and that its uptake is involved in the MHC I antigen presentation pathway (see Basu *et al* Immunity 2001 Mar;14(3):303-13, see abstract only & Binder *et al* J Biol Chem 2001 May;276(20):17163-17171).

The amount of direction or guidance present and the presence or absence of working examples: The examples of the instant application are drawn to the identification of CD91 or alpha 2 macrolobulin receptor as the receptor for HSPs, specifically HSP90, HSP70, gp96 and calreticulin. However, nowhere in the form of working examples does the instant application teach to one of skill in the art how to utilize the interaction of CD91/α2m receptor with HSPs to treat or let alone prevent autoimmune disease, proliferative disorders, or infectious disease. Further, it is not clear as to how one of skill in the art would be able to treat or prevent proliferative disorders or infectious diseases through the modulation of CD91/ α2m receptor with an anti-CD91 antibody. First, the state of the art teaches that the interaction of CD91/ α2m receptor and HSPs

are involved in antigen presentation through the MHC I pathway. The specification has only taught of a blocking anti-CD91 antibody, that was able to inhibit the presentation of peptides non-covalently associated with HSPs. If for example, the purpose of the HSP-peptide complex is to present a tumor associated antigen or peptide to an APC and an antibody as described in the specification was used treat cancer or a cell proliferative disorder, the peptide would never be presented because the antibody would prevent the peptide from entering the antigen presentation pathway. One of skill in the art may be able to fathom a method for treating autoimmune disease, through the blockade of self peptide from being presented to the immune system, but if such an method was used to treat cell proliferative disorders or infectious diseases, the problem will only be enhanced and not treated, such as in a bacterial infection. However, such a method of treating autoimmune disease would still require undue experimentation by one of skill in the art because the specification has not taught how to accomplish such a method. Secondly, as stated *supra*, the antibody disclosed is a blocking antibody, it would require one of skill in the art undue experimentation to screen and find an enhancing or catalytic antibody that is capable of acting as an agonist thereby increasing the activity of the receptor for HSPs. Thridly, the specification has not taught one of skill in the art how to utilize, treat, or especially prevent diseases through the manipulation of the CD91/α2m receptor – HSPs interaction. The specification has only taught that blocking of the receptor is capable of preventing peptide presentation on MHC I, but this is not a specific treatment method, only an *in vitro* experiment teaching the ability of a peptide to be blocked or presented by a MHC I molecules. Furthermore, with respect to methods

of preventing disease, one of skill in the art would require undue experimentation to accomplish prevention because the population of subjects or patients to be treated or vaccinated is not known. Surely, one of skill in the art would not be able to predetermine such a population because one of skill does not know who would be at risk of developing cell proliferative disorders, infectious diseases, and or autoimmune diseases. And finally, evening assuming, *arguendo*, that the disclosed invention was to treat a cell proliferative disorder, an infectious disease or an autoimmune disorder, all the diseases that are claimed have different etiologies, different mechanisms of control and have potentially different methods of treatment that may require different interactions or even multiple interactions to be blocked or modulated, all of which have not be taught by way of working examples in the instant specification.

The breadth of the claims and the quantity of experimentation needed: Given the lack of an enabling disclosure, and the broad range of disease encompassed by the method, it would require undue experimentation by one of skill in the art to be able to practice the invention commensurate in scope with the claims.

Conclusion

16. No claim is allowed. This action is made **NON-FINAL** in view of the new rejections set forth in the instant Office action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher H Yaen whose telephone number is 703-305-3586. The examiner can normally be reached on Monday-Friday 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Christopher Yaen
Art Unit 1642
December 1, 2002